

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (currently amended): A method of parallel analysis of biological specimens, comprising:

- obtaining a plurality of donor specimens;
- placing each donor specimen in an assigned x-y coordinate location in a recipient array;
- obtaining a plurality of substantial copies of the recipient array in a manner that each substantial copy contains a plurality of donor specimens that maintain their assigned x-y coordinate locations;
- placing each substantial copy of each recipient array on a separate support;
- subjecting a first substantial copy of the recipient array on a first support to a first assay;
- subjecting at least one successive second substantial copy of the recipient array on at least one second support to at least one second assay, wherein the first assay is different than the second assay and at least one of the first or second assay comprises at least one immunological analysis and at least one of the first or second assay comprises at least one nucleic acid hybridization;
- comparing the results of the first assay and at least one second assay in corresponding assigned x-y coordinate locations of the first substantial copy and the at least one successive second substantial copy to determine if there are correlations between the results of the first assay and at least one second assay at each assigned x-y coordinate location; and
- analyzing the correlations to:
  - identify a prognostic marker for a disease;
  - prioritize targets for drug development;
  - assess or select therapy for a disease type;
  - find a biochemical target for medical therapy;
  - determine the frequency of a target in pathological and normal physiological tissue;
  - identify therapeutic targets that are expressed in pathological tissue relative to normal physiological tissue;
  - compare the expression or presence of a target at the DNA, RNA and protein level; or
  - identify, validate, and prioritize targets that are defined by utilizing bioinformatic

analyses.

Claim 2 (original): The method of claim 1, wherein the donor specimen is obtained by boring an elongated sample from the donor specimen, which is placed in the assigned location in the recipient array.

Claim 3 (canceled).

Claim 4 (original): The method of claim 1, wherein the donor specimen is from a population of cells.

Claim 5 (previously presented): The method of claim 1, wherein the donor specimen is from a hematological or cytological preparation.

Claim 6 (previously presented): The method of claim 1, wherein placing the donor specimen in an assigned location in the recipient array comprises forming an elongated receptacle in a recipient block, obtaining an elongated donor specimen, and placing the elongated donor specimen in the elongated receptacle of the recipient block, and obtaining a plurality of copies comprises sectioning the array transverse to the elongated donor specimen.

Claim 7 (previously presented): The method of claim 6, wherein the elongated donor specimen is placed in a receptacle having a cross-sectional size and shape complementary to a cross-sectional size and shape of the elongated donor specimen.

Claim 8 (previously presented): The method of claim 7, wherein forming the elongated receptacle comprises forming a cylindrical bore in the recipient block, and the donor specimen is obtained by boring a cylindrical tissue specimen from a donor block, wherein a diameter of the elongated receptacle is substantially the same as a diameter of the donor specimen.

Claim 9 (previously presented): The method of claim 1, further comprising associating a clinical characteristic with each assigned location in the recipient array.

Claims 10-11 (canceled).

Claim 12 (previously presented): The method of claim 1, further comprising determining whether there are correlations between clinical characteristics, associated with each assigned location, and the results of the first assay and the at least one second assay.

Claim 13 (canceled).

Claim 14 (previously presented): The method of claim 12, wherein the clinical characteristics are one or more of clinical course, treatment response, patient age, tumor grade, tumor size, node status, and receptor status.

Claim 15 (canceled).

Claim 16 (currently amended): A method of parallel analysis of substantially identical arrays of tissue specimens, comprising:

obtaining a plurality of elongated donor sample cores from at least one biological specimen;

boring receptacle cores from a recipient embedding medium to form an array of elongated receptacles;

placing the donor sample cores in the elongated receptacles at assigned x-y coordinate locations in the array;

sectioning the recipient embedding medium transverse to the elongated receptacles to obtain a plurality of consecutive cross-sections of the donor sample cores in the array, while maintaining the assigned x-y coordinate locations in the array in the consecutive cross-sections;

placing each cross-section on a separate support;

subjecting a first cross-section on a first support to a first assay;

subjecting at least one second consecutive cross-section on at least one second support to at least one second assay, wherein the first assay is different from the second assay and at least one of the first or second assay comprises at least one immunological analysis and at least one of the first or second assay comprises at least one nucleic acid hybridization;

comparing a result of the first assay and the at least one second assay in corresponding assigned x-y coordinate locations of different consecutive cross-sections to determine if there are correlations between the results of the first assay and the at least one second assay at each assigned x-y coordinate location; and

analyzing the correlations to:

- identify a prognostic marker for a disease;
- prioritize targets for drug development;
- assess or select therapy for a disease type;
- find a biochemical target for medical therapy;
- determine the frequency of a target in pathological and normal physiological tissue;
- identify therapeutic targets that are expressed in pathological tissue relative to normal physiological tissue;
- compare the expression or presence of a target at the DNA, RNA and protein level; or
- identify, validate, and prioritize targets that are defined by utilizing bioinformatic analyses.

Claim 17 (previously presented): The method of claim 16, further comprising comparing the results of the first assay and the at least one second assay at each assigned location to clinical information about the biological specimen at the assigned location.

Claim 18 (previously presented): The method of claim 17, wherein the biological specimen is a tissue specimen from a tumor.

Claim 19 (canceled)

Claim 20 (previously presented): The method of claim 17, wherein the clinical information is one or more of clinical course, treatment response, patient age, tumor grade, tumor size, node status, and receptor status.

Claim 21 (canceled).

Claim 22 (previously presented): The method of claim 16, wherein the elongated donor sample core is a substantially cylindrical core that has a diameter that is less than 1 mm.

Claim 23 (canceled).

Claim 24 (previously presented): The method of claim 1, further comprising using a nucleic acid microarray to identify a biomarker to be used in the first assay or the second assay, wherein the nucleic acid microarray comprises an arrangement of nucleic acid in assigned locations on a matrix.

Claim 25 (previously presented): The method of claim 24, wherein the nucleic acid microarray is a cDNA or oligonucleotide microarray.

Claim 26 (previously presented): The method of claim 25, wherein the biomarker is selected by a high throughput immunological or genetic analysis.

Claim 27 (previously presented): The method of claim 24, wherein the biomarker comprises a marker for gene expression.

Claim 28 (previously presented): The method of claim 26, wherein the biomarker comprises a structural or numerical alteration of a chromosome, chromosomal region, gene, gene fragment or locus, or a gene function alteration.

Claim 29 (previously presented): The method of claim 1, wherein comparing the results comprises determining if there is an alteration of a gene by examining a marker for protein expression or other gene alteration.

Claim 30 (previously presented): The method of claim 29, wherein the alteration of protein expression is determined by an immunologic analysis.

Claim 31 (previously presented): The method of claim 29, wherein the alteration is an overexpression of vimentin in renal cell carcinoma, or an overexpression of IGFBP2 in human prostate

cancer, or an overexpression of PDGFB in breast, lung, colon, testicular, endometrial or bladder cancer.

Claim 32 (currently amended): A method of analyzing genetic changes or gene expression in a tissue specimen, comprising:

screening multiple genes in a biological specimen, with a nucleic acid array that detects which genes are abnormally expressed in the biological specimen, wherein the nucleic acid array comprises an arrangement of nucleic acid in assigned locations on a matrix at least hundreds of different nucleic acid sequences affixed to the surface of a support and arrayed in assigned locations in the shape of a grid; and

screening multiple biological specimens in a biological specimen microarray with a nucleic acid probe to detect which genes are abnormally expressed in the biological specimens;

wherein the result of screening multiple genes is used to select the nucleic acid probe to screen the multiple biological specimens, or wherein the result of screening multiple biological specimens is used to select the nucleic acid array that detects which genes are abnormally expressed.

Claim 33 (previously presented): The method of claim 32, wherein screening multiple genes comprises performing a high throughput genomic technique.

Claim 34 (previously presented): The method of claim 32, wherein the high throughput genomic technique is selected from the group of cDNA or genomic DNA sequencing, protein sequencing, RDA, differential display, subtractive hybridization, SAGE, hybridization based sequencing, and cDNA and oligonucleotide arrays.

Claim 35 (previously presented): The method of claim 32, wherein screening multiple genes to determine which genes are abnormally expressed comprises searching databases and other biomedical sources of information.

Claim 36 (previously presented): The method of claim 32, wherein screening the multiple genes comprises using a cDNA array to determine which genes are abnormally expressed.

Claim 37 (previously presented): The method of claim 32, wherein screening the multiple genes comprises providing a DNA array which is assayed for a gene amplification, deletion, mutation, polymorphism, methylation change or other alternation of gene structure or function, or a genetic or molecular marker that reflects this change.

Claim 38 (previously presented): The method of claim 37, wherein the DNA array is a microarray that contains target loci that undergo differential expression in cancer.

Claim 39 (previously presented): The method of claim 32, wherein screening multiple genes obtained from a single biological specimen comprises hybridizing nucleic acid molecules associated with a cell with the DNA array that contains target loci that undergo differential expression, and determining which target loci indicate differential expression of a gene in the cell.

Claim 40 (previously presented): The method of claim 39, further comprising selecting a target locus that undergoes differential expression, providing a probe that includes or is complementary to at least a portion of the target locus, and using the probe to screen the multiple biological specimens.

Claim 41 (previously presented): The method of claim 32, wherein the biological specimen is a tissue specimen.

Claim 42 (previously presented): The method of claim 41, wherein the tissue specimen is a tumor specimen.

Claims 43-45 (canceled).

Claim 46 (previously presented): The method of claim 1, wherein identifying a prognostic marker for cancer comprises selecting a marker associated with a poor clinical outcome.

Claim 47 (previously presented): The method of claim 1, wherein selecting therapy for the subject comprises selecting an antineoplastic therapy that is associated with a particular biological analysis outcome.

Claim 48 (previously presented): The method of claim 47, wherein the particular biological analysis outcome is an oncogene amplification, deletion, translocation, mutation or other genetic rearrangement which is correlated with a clinical response to a particular therapy.

Claim 49 (previously presented): The method of claim 1, wherein the donor specimens are specimens from one or more tumors.

Claim 50 (previously presented): The method of claim 49, wherein the donor specimens are from breast cancer tumors.

Claim 51 (previously presented): The method of claim 49, wherein the donor specimens are specimens from a plurality of tumors all of the same organ or histologic type.

Claim 52 (previously presented): The method of claim 48, wherein the donor specimens are specimens from a plurality of tumors from different organs or tissue types.

Claim 53 (currently amended): A method of analyzing cellular specimens in a matrix, with the specimens positioned at predetermined known x-y coordinate positions, such that when multiple copies of the matrix are provided, a two dimensional array of specimens is presented on each copy, with each specimen at a predetermined x-y coordinate position in the matrix, and wherein each matrix has a third dimension so that when sequential copies of the matrix are provided, the specimens maintain a predetermined relationship in the array, the method comprising exposing a first copy of the matrix on a first support to a first agent which interacts with the specimens of the array and exposing at least one successive sequential second copy of the matrix on at least one second support to at least one second agent that is different than the first agent wherein at least one of the first agent or the second agent comprises an antibody and at least one of the first agent or the second agent comprises a nucleic acid probe, to identify those specimens which share a common biological property, and analyzing the specimens that share the common biological property to:

- identify a prognostic marker for a disease;
- prioritize targets for drug development;



assess or select therapy for a disease type;  
find a biochemical target for medical therapy;  
determine the frequency of a target in pathological and normal physiological tissue;  
identify therapeutic targets that are expressed in pathological tissue relative to normal physiological tissue;  
compare the expression or presence of a target at the DNA, RNA and protein level; or  
identify, validate, and prioritize targets that are defined by utilizing bioinformatic analyses.

Claim 54 (previously presented): The method of claim 53, wherein the specimens are provided in an elongated form, and multiple copies of the matrix are made by cutting sections from a three dimensional array into predetermined sections, such that as sequential sections of the matrix are cut, the specimens maintain the predetermined relationship.

Claim 55 (previously presented): The method of claim 53, wherein the common biological property is a morphologic or molecular characteristic.

Claim 56 (previously presented): The method of claim 53, wherein the common biological property is a presence or absence, or altered level of expression, of a gene or protein, alteration of copy number, structure or function of a gene, genetic locus, chromosomal region or chromosome.

Claim 57 (previously presented): The method of claim 54, wherein the common biological property is a specific reaction with an antibody specific for a specimen of interest.

Claim 58 (previously presented): The method of claim 53, wherein the common biological property is correlated with another characteristic of the specimens.

Claim 59 (previously presented): The method of claim 58, wherein the other characteristic of the specimens includes clinical information about a subject from whom each specimen was taken.

Claim 60 (previously presented): The method of claim 59, wherein the clinical information

includes one or more of clinical course, treatment response, histological type or grade, tumor stage, and age and sex of the subject from whom each specimen was taken.

Claim 61 (previously presented): The method of claim 53, wherein the cellular specimen is a tissue specimen.

Claim 62 (previously presented): The method of claim 53, wherein the cellular specimen is a cellular suspension.

Claim 63 (previously presented): The method of claim 62, wherein the specimen is a liquid cellular specimen that has been converted into a solid cellular specimen.

Claims 64-65 (canceled).

Claim 66 (previously presented): The method of claim 53, further comprising exposing a gene array to a candidate specimen, and selecting a candidate probe for the specimen array.

Claim 67 (previously presented): The method of claim 53, wherein the common biological property is her-2 status, and the method further comprises selecting a therapy based on her-2 status.

Claim 68 (previously presented): The method of claim 63, wherein the specimens comprise a tissue from a model or transgenic organism.

Claim 69 (previously presented): The method of claim 68, wherein the specimens comprise tissue from the model or transgenic organism at different stages of development.

Claim 70 (previously presented): The method of claim 53, wherein the specimens comprise animal, yeast or bacterial cells.

Claim 71 (previously presented): The method of claim 70, wherein the cells are in a liquid suspension which is applied to a surface of a support.

Claim 72 (previously presented): The method of claim 71, wherein the liquid suspension is from a body fluid.

Claim 73 (previously presented): The method of claim 72, wherein the body fluid is selected from the group of a needle aspiration, a cytology specimen, urine, and ascitic fluid.

Claim 74 (previously presented): The method of claim 70, wherein the cells comprise a sample of a liquid malignancy.

Claim 75 (previously presented): The method of claim 74, wherein the liquid malignancy comprises a hematological malignancy.

Claim 76 (previously presented): The method of claim 70, wherein the cells are from one or more cell lines.

Claim 77 (previously presented): The method of claim 53, wherein the specimens comprise specimens from one or more tumors at different stages of progression.

Claim 78 (previously presented): The method of claim 77, wherein the one or more tumors are prostate cancer tumors.

Claims 79-85 (canceled).

Claim 86 (previously presented): The method of claim 49, wherein the donor specimens are specimens from one or more tumors selected from the group of prostate and bladder cancer.

Claim 87 (previously presented): The method of claim 1, wherein the method does not destroy the morphology or cellular structure of the donor specimens.

Claim 88 (currently amended): A method of parallel analysis of biological specimens,

comprising:

- obtaining a plurality of donor specimens;
- placing each donor specimen in an assigned x-y coordinate location in a recipient array;
- obtaining a plurality of sections of the recipient array in a manner that each section contains a plurality of donor specimens that maintain their assigned x-y coordinate locations;
- placing each section of each recipient array on a separate support;
- subjecting a first section of the recipient array on a first support to a first assay;
- subjecting at least one successive second section of the recipient array on at least one second support to at least one second assay, wherein the first assay is different compared to the second assay and at least one of the first or second assay comprises at least one immunological analysis and at least one of the first or second assay comprises at least one nucleic acid hybridization;
- comparing the results of the first assay and the at least one second assay in corresponding assigned x-y coordinate locations of the first section and the at least one second section to determine if there are correlations between the results of the first assay and the at least one second assay at each assigned x-y coordinate location; and
- analyzing the correlations to:
  - identify a prognostic marker for a disease;
  - prioritize targets for drug development;
  - assess or select therapy for a disease type;
  - find a biochemical target for medical therapy;
  - determine the frequency of a target in pathological and normal physiological tissue;
  - identify therapeutic targets that are expressed in pathological tissue relative to normal physiological tissue;
  - compare the expression or presence of a target at the DNA, RNA and protein level; or
  - identify, validate, and prioritize targets that are defined by utilizing bioinformatic analyses.

Claim 89 (previously presented): The method of claim 1, further comprising correlating additional information concerning the donor specimens with the assay correlation, wherein the additional information is at least one of patient demographics, clinical tumor staging data, and patient follow-up data.

Claim 90 (canceled).

Claim 91 (previously presented): The method of claim 1, further comprising obtaining the donor specimens from a predetermined morphologically defined region of a tumor.

Claim 92 (previously presented): The method of claim 1, further comprising obtaining the donor specimens from a predetermined cell structure.

Claims 93-97 (canceled).

Claim 98 (previously presented): The method of claim 2, wherein the elongated sample is a substantially cylindrical core that has a diameter that is less than 1 mm.

Claim 99 (previously presented): The method of claim 2, wherein the elongated sample is a substantially cylindrical core that has a diameter of 0.3 to 2.0 mm and a length of 1 to 4 mm.

Claim 100 (previously presented): The method of claim 16, wherein the elongated donor sample core is a substantially cylindrical core that has a diameter of 0.3 to 2 mm.

Claims 101-102 (canceled).

Claims 103-113 (not entered).

Claims 114-115 (canceled)

Claim 116 (previously presented): The method of claim 53, wherein at least the first agent or the second agent comprises a probe for an oncogene.

Claim 117 (previously presented): The method of claim 16, wherein the donor samples cores are obtained from plurality of specimens representing a cancer progression and the assays are

performed to determine the presence or absence of gene or protein expression.

Claim 118 (previously presented): The method of claim 53, wherein the specimens are representative of a cancer progression and the agents are selected to determine the presence or absence of gene or protein expression.

Claims 119-123 (canceled)